



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,118	02/25/2002	Didier Lefevre	20198/0059	8544

7590 02/23/2006

George R. Pettit  
Connolly Bove Lodge & Hutz LLP  
Suite 800  
1990 M Street, N.W.  
Washington, DC 20036-3425

EXAMINER

GABEL, GAILENE

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/081,118	<b>Applicant(s)</b> LEFEVRE ET AL.	
	<b>Examiner</b> Gailene R. Gabel	<b>Art Unit</b> 1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 November 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 3-6 and 9-21 is/are pending in the application.
- 4a) Of the above claim(s) 12-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3-6, 9-11 and 19-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 3-6 and 9-21 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 22, 2005 has been entered.

### ***Amendment Entry***

2. Applicant's amendment and arguments, filed on November 22, 2005, is acknowledged and has been entered. Claims 1, 2, 7, and 8 have been cancelled. Claims 3-6, 11, and 19 have been amended. Claims 20 and 21 have been added. Claims 12-18 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Accordingly, claims 3-6 and 9-21 are pending. Claims 3-6, 9-11, and 19-21 are under examination.

### ***Withdrawn Rejections***

3. All rejections not reiterated herein, have been withdrawn.

Art Unit: 1641

4. The rejections of claims 1, 2, 7, and 8 are now moot in light of Applicant's cancellation of the claims.

5. In light of Applicant's amendment and arguments, the rejection of claims 3-6, 9-11 under 35 U.S.C. 102(e) as being anticipated by Deka et al. (US 6,271,035) is hereby, withdrawn.

6. In light of Applicant's amendment and arguments, the rejection of claims 3-6, 9-11 under 35 U.S.C. 102(e) as being anticipated by Sakata (US 5,496,734) is hereby, withdrawn.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 5, 19, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 remains ambiguous in reciting, "to enhance a fluorescent signal from the stain", because it is unclear what fluorescent signal is being enhanced in relation to the sample. Does Applicant intend, "to enhance the fluorescent signal from the stain bound to the intracellular ribonucleic acid in the unlyzed cells.

Claim 19 lacks antecedent basis for the recitation of, "the nucleic acids" in the last line.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 3-6, 9-11, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakata (US 5,496,734) in view of Haas et al. (Cation-Anion Cotransport, Methods in Enzymology, 173: 280-91 (1989)) (Abstract).

Sakata discloses a reagent for identifying, counting, and classifying blood cells. The reagent comprises a lysing agent which is quaternary ammonium salts at a concentration that lyses erythrocytes and a fluorescent stain that can permeate through permeabilized cell membrane of nucleated unlysed cells (leucocytes) so as to incorporate with and label intracellular nucleic acids of the unlysed nucleated cells (see column 6, line 64 to column 7, lines 1-67, column 8, lines 1-12, and especially column 10, lines 44-62). According to Sakata, nonionic surfactants may also be added to the reagent to control the effects of ionic surfactants toward cell membrane (see column 9, line 14 to column 10, line 4). Sakata provides that the surfactant may function by removing part of substances which constitute cell membrane; thus yielding pores in the cell membrane to allow passage of substances such as stain into the cell (see column 10, line 63 to column 11, line 8). Stains used with the reagent include Thiazole Orange, Acridine Orange, ethidium bromide, and propidium bromide (see column 8, lines 18-29). Sakata teaches that alcohol can be added as fixing agent to minimize loss of

Art Unit: 1641

cytoplasms and granules and to optimize degree of damage of the cell membranes. According to Sakata, formaldehyde and gluteraldehyde are also used as fixing agents (see column 10, lines 10-39 and column 2, lines 13-19). The reagent further includes anticoagulant and buffer (see column 8, line 64 to column 9, line 13).

Sakata et al. differ from the instant invention in failing to teach incorporation of ionophore into a reagent for identifying and counting nucleated blood cells.

Haas et al. provide use of valinomycin in cation-anion cotransport, as an ionophore for increasing permeability of cell membrane in red blood cells to specific elements, i.e. sodium and potassium. Haas et al. show investigations of valinomycin with different cells and successfully demonstrated that there is electroneutrality of ( $\text{Na}^+ + \text{K}^+ + 2\text{Cl}^-$ ) cotransport in MDCK cells.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate valinomycin as an ionophore as taught by Haas into the reagent taught by Sakata for use in identifying, counting, and classifying blood cells, because Haas specifically provided that valinomycin is capable of increasing permeability of cell membrane in red blood cells; hence enhancing penetration of stain into intracellular red blood cell environment to thus allow more accurate detection, identification, and classification of nucleated blood cells in a sample.

### ***Response to Arguments***

9. Applicant's arguments with respect to claims 3-6, 9-11, and 19-21 have been considered but are moot in view of the new grounds of rejection.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel  
Patent Examiner  
Art Unit 1641  
February 16, 2006

